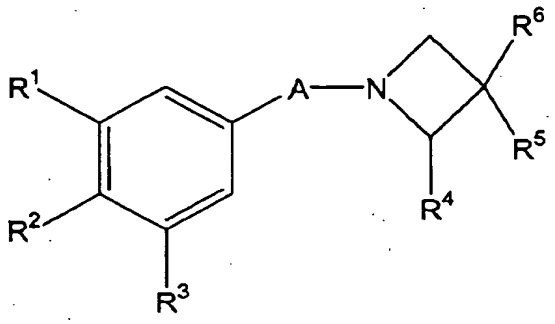
Claims:

1. Substituted Azetidine compounds of general formula I,



wherein

A represents a –C=O-moiety, a -CH_2-moiety, a –CH_2-C=O-moiety bonded to the azetidine ring via its carbonyl carbon atom, or a –O-C(=O)-moiety bonded to the azetidine ring via its carbonyl carbon atom,

R^1, R^3, identical or different, represent a hydrogen atom or a linear or branched, saturated or unsaturated C_{1-4}-aliphatic group,

R^2 represents a hydrogen atom, a hydroxyl group or a C_{1-3}-alkoxy group,

or R^1 and R^2 or R^2 and R^3 together form an –O-CH_2-CH_2-chain, which is optionally substituted with one or more methyl groups

with the proviso that R^1, R^2 and R^3 do not identically represent a hydrogen atom, and if A represents a -CH_2-moiety, then at least two of the residues R^1, R^2 and R^3 do not identically represent a hydrogen atom,

R^4 represents a hydrogen atom, an optionally at least mono-substituted aryl group, or a linear or branched, saturated or unsaturated aliphatic group, which may be substituted by one or more substituents independently selected from the group consisting of hydroxy, fluorine, chlorine, bromine, branched or unbranched C_{1-4}-alkoxy, branched or unbranched C_{1-4}-perfluoroalkoxy and branched or unbranched C_{1-4}-perfluoroalkyl,

R^5 represents a hydrogen atom, a halogen atom, a hydroxyl group, a linear or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic group, an $-OR^7$-moiety, -an $-NH_2$-moiety, a $-CO-NH_2$-moiety, an $-NH-CO-R^8$-moiety, an $-N(OH)-CO-NH_2$-moiety, an $-O(CH_2)_{1-4}-ONO_2$-moiety, an optionally at least mono-substituted aryl group, or a carboxy-group,

R^6 represents a hydrogen atom, a halogen atom, a hydroxyl group, a linear or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic group, an $-OR^9$-moiety, -an $-NH_2$-moiety, a $-CO-NH_2$-moiety, an $-NH-CO-R^{10}$-moiety, an $-N(OH)-CO-NH_2$-moiety, an optionally at least mono-substituted aryl group, or a carboxy-group,

R^7, R^8, R^9, R^{10}, independent from one another, represent a linear or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic group,

with the provisos

that if A represents a $-(C=O)$-moiety, R^4 represents a hydrogen atom and one of the residues R^5 and R^6 represents a hydrogen atom, then the other one of these residues R^5 and R^6 does not represent an $-NH_2$-moiety, a $-CONH_2$-moiety, or a methyl group, which is substituted by an $-NH_2$-moiety or an azaheterocycle, and

if A represents a –C=O-moiety, a $–CH_2$-C=O-moiety bonded to the azetidine ring via its carbonyl carbon atom, or a –O-C(=O)-moiety bonded to the azetidine ring via its carbonyl carbon atom and one of the residues R^5 and R^6 represents a hydrogen atom or an optionally at least mono-substituted, linear or branched, saturated or unsaturated aliphatic group, then the other one of these residues R^5 and R^6 does not represent an $–NH_2$- or a COOH–moiety,

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

2. Compounds according to claim 1, characterized in that R^1 and R^3, identical or different, represent a hydrogen atom or a linear or branched C_{1-4}-alkyl group.

3. Compounds according to claim 1 or 2, characterized in that R^1 and R^3 are identical and represent a C_{1-4}-alkyl group, preferably a C_{3-4} alkyl group, more preferably an iso-propyl group or a tert.-Butyl group.

4. Compounds according to one or more of claims 1-3, characterized in that R^2 represents a hydrogen atom, a hydroxyl group or a methoxy group.

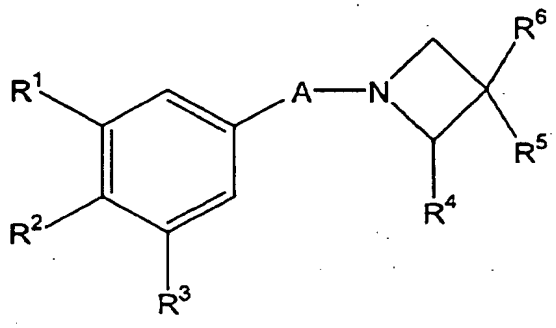
5. Compounds according to one or more of claims 1-4, characterized in that R^4 represents a hydrogen atom, an optionally at least mono-substituted phenyl group, or a linear or branched, saturated or unsaturated C_{1-6} aliphatic group, whereby said aliphatic group may be substituted by one or more substituents independently selected from the group consisting of hydroxy, fluorine, chlorine, bromine, branched or unbranched C_{1-4}-alkoxy, branched or unbranched C_{1-4}-perfluoroalkoxy and branched or unbranched C_{1-4}-perfluoroalkyl, preferably a hydrogen atom, a methyl group or an unsubstituted phenyl group.

6. Compounds according to one or more of claims 1-5, characterized in that R^5 represents a hydrogen atom, a halogen atom, a hydroxyl group, a linear or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6} aliphatic group, an $-NH_2$-moiety, a $-CO-NH_2$-moiety, an $-NH-CO-R^8$-moiety, an $-N(OH)-CO-NH_2$-moiety, an $-O(CH_2)_4-ONO_2$-moiety, an optionally at least mono-substituted phenyl group, or a carboxy-group, preferably a hydrogen atom, a bromine atom, a hydroxyl group, an $-NH_2$-moiety, a $-CO-NH_2$-moiety, an $-NH-CO-R^8$-moiety, an $-N(OH)-CO-NH_2$-moiety, an $-O(CH_2)_4-ONO_2$-moiety, an unsubstituted phenyl group, or a carboxy-group.

7. Compounds according to one or more of claims 1-6, characterized in that R^6 represents a hydrogen atom, a halogen atom, a hydroxyl group, a linear or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6} aliphatic group, an $-NH_2$-moiety, a $-CO-NH_2$-moiety, an $-NH-CO-R^8$-moiety, an $-N(OH)-CO-NH_2$-moiety, an optionally at least mono-substituted phenyl group, or a carboxy-group, preferably a hydrogen atom, a hydroxyl group or a methyl group.

8. Compounds according to one or more of claims 1-7, characterized in that R^7, R^8, R^9, R^{10}, independent from one another, represent a linear or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6} aliphatic group, preferably a linear or branched C_{1-6} alkyl group, more preferably a methyl group or an ethyl group.

9. Compounds according to one ore more of claims 1-8 of general formula I,



wherein

A represents a –C=O-moiety, a -CH_2-moiety, a –CH_2-C=O-moiety bonded to the azetidine ring via its carbonyl carbon atom, or a –O-C(=O)-moiety bonded to the azetidine ring via its carbonyl carbon atom,

R^1, R^3 both identically represent an iso-propyl group or a tert.-butyl group,

R^2 represents a hydrogen atom, a hydroxyl group or a methoxy group,

or R^1 and R^2 or R^2 and R^3 together form an –O-CH_2-$C(CH_3)_2$-chain, whereby the oxygen atom of said chain is bonded to the 4-position of the phenyl ring,

R^4 represents a hydrogen atom, a methyl group or an unsubstituted phenyl group,

R^5 represents a bromine atom, a hydroxyl group, -an –NH_2-moiety, a –CO-NH_2-moiety, an –NH-CO-CF_3-moiety, an –N(OH)-CO-NH_2-moiety, an -$O(CH_2)_4ONO_2$-moiety, an unsubstituted phenyl group, or a carboxy-group,

R^6 represent a hydrogen atom, a methyl group or a hydroxyl group,

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

10. Compounds according to one or more of claims 1-9 selected from the group consisting of

[1] (3,5-di-tert-butyl-4-hydroxy-phenyl)-(3-hydroxy-azetidin-1-yl)-methanone;

[2] (3,5-di-tert-butyl-phenyl)-(3-hydroxy-azetidin-1-yl)-methanone;

[3] (3,5-di-tert-butyl-4-hydroxy-phenyl)-(3-hydroxy-3-methyl-azetidin-1-yl)-methanone;

[4] (3,5-di-tert-butyl-4-hydroxy-phenyl)-(3-hydroxy-2-methyl-azetidin-1-yl)-methanone;

[7] (3-Bromo-azetidin-1-yl)-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

[9] (3,5-di-tert-butyl-4-methoxy-phenyl)-(3-hydroxy-azetidin-1-yl)-methanone;

[10] (3-hydroxy-azetidin-1-yl)-(4-hydroxy-3,5-diisopropyl-phenyl)-methanone;

[11] (3,5-di-tert-butyl-phenyl)-[3-(4-nitrooxy-butoxy)-azetidin-1-yl]-methanone;

[12] (3,5-di-tert-butyl-4-hydroxy-phenyl)-(3-hydroxy-2-phenyl-azetidin-1-yl)-methanone;

[13] (3,5-di-tert-butyl-4-hydroxy-phenyl)-(3-hydroxy-3-phenyl-azetidin-1-yl)-methanone;

[14] (7-tert-butyl-3,3-dimethyl-2,3-dihydro-benzofuran-5-yl)-(3-hydroxy-azetidin-1-yl)-methanone;

[15] [1-(3,5-di-tert-butyl-4-hydroxy-benzyl)-azetidin-3-yl]-N-hydroxy-urea;

[16] N-[1-(3,5-di-tert-butyl-4-hydroxy-benzoyl)- (2S,3R)-2-methyl-azetidin-3-yl]-2,2,2-trifluoro-acetamide;

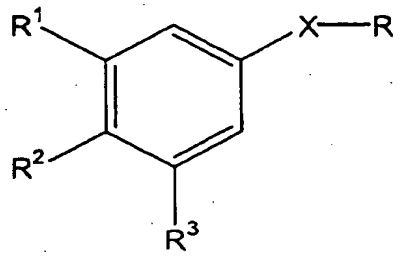
[17] 1-(3,5-di-tert-butyl-4-hydroxy-benzyl)-azetidin-3-ol;

[18] 2-(3,5-di-tert-butyl-4-hydroxy-phenyl)-1-(3-hydroxy-azetidin-1-yl)-ethanone;

[19] (3-hydroxy-azetidine-1-carboxylic acid)-3,5-di-tert-butyl-phenyl ester

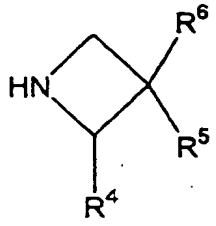
optionally in form of a corresponding salt or a corresponding solvate.

11. Process for the preparation of substituted azetidine compounds of general formula I according to one or more of claims 1-10, characterized in that at least one compound of general formula II,



II

wherein R^1-R^3 have the meaning according to one or more of claims 1-10, X represents a bond or an $-(CH_2)$-moiety and R represents a carboxy group or an activated carbonyl group, is reacted with at least one compound of general formula III,

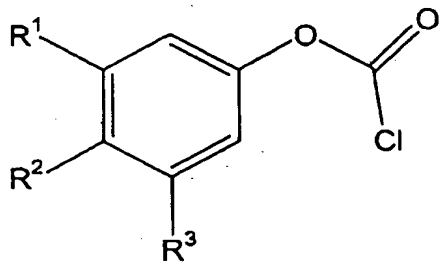


III

optionally in the form of a corresponding salt, wherein R^4-R^6 have the meaning according to one or more of claims 1-10, to yield a compound of general formula I according to one or more of claims 1-10, wherein A represents a –(C=O)-moiety or an -(CH_2)-CO-moiety, which is optionally purified and/or optionally isolated,

and optionally at least one compound of general formula I according to one or more of claims 1-10, wherein A represents a –(C=O)-moiety is reduced to yield at least one compound of general formula I according to one or more of claims 1-10, wherein A represents a –(CH_2)-moiety, which is optionally purified and/or isolated,

or at least one compound of general formula IV,



IV

wherein R^1-R^3 have the meaning according to one or more of claims 1-10, is reacted with at least one compound of general formula III given above, to yield at least one compound of general formula I according to one or more of claims 1-

10, wherein A represents an O-(C=O)-moiety, and said compound is optionally purified and/or optionally isolated.

12. Medicament comprising at least one substituted azetidine compound according to one or more of claims 1-10 and optionally one or more pharmaceutically acceptable excipients.

13. Medicament according to claim 12 for the inhibition of Cyclooxygenase-1, for the prophylaxis and/or treatment of Cyclooxygenase-1 related disorders, for the inhibition of Cyclooxgenase-2 and/or for the prophylaxis and/or treatment of Cyclooxygenase-2 related disorders.

14. Medicament according to claim 12 or 13 for the prophylaxis and/or treatment of pain, for the prophylaxis and/or treatment of inflammation and/or for the prophylaxis and/or treatment of inflammation related disorders, whereby said inflammation-related disorders may preferably be selected from the group consisting of arthritis, rheumatoid arthritis, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus, juvenile arthritis, rheumatic fever, symptoms associated with influenza or other viral infections, common cold, lower back pain, neck pain, dysmenorrhea, headache, toothache, sprains, strains, myositis, neuralgia, synovitis, gout, ankylosing spondylitis, bursitis, edema, inflammations following dental procedures, inflammations following dental procedures, vascular diseases, migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodkin`s disease, sclerodoma, type I diabetes, myasthenia gravis, sarcoidosis, nephrotic syndrome, Behcet`s syndrome, polymyositis, gingivitis, hypersensivity, conjunctivitis, swelling ocurring after injury and myocardia ischemia, for the prophylaxis and/or treatment of asthma, for the prophylaxis and/or treatment of bronchitis, for the prophylaxis and/or treatment of tendinitis, for the prophylaxis and/or treatment of bursitis, for the prophylaxis and/or treatment of skin related conditions, whereby said skin related conditions may preferably be selected from the group consisting of psoriasis, eczema, burns and dermatitis, for the prophylaxis and/or treatment of gastrointestinal disorders, whereby said gastrointestinal disorders may preferably be selected from the group consisting of inflammatory bowel disease, Crohn`s disease, gastritis,

irritable bowel syndrome and ulcerative colitis, or for treatment of fever, or for the prophylaxis and/or treatment of cancer or a cancer-related disorders, whereby said cancer or related disorder may preferably be selected from the group consisting of brain cancer, bone cancer, epithelial cell-derived neoplasia (epithelial carcinoma), basal cell carcinoma, adenocarcinoma, gastrointestinal cancer, lip cancer, colon cancer, liver cancer, bladder cancer, pancreas cancer, ovary cancer, cervical cancer, lung cancer, breast cancer, skin cancer, squamous cell cancer, prostate cancer, renal cell carcinoma and other known cancers that effect epithelial cells throughout the body, for the prophylaxis and/or treatment of polyps, for the prophylaxis and/or treatment of angiogenesis mediated disorders, preferably selected from the group consisting of metastasis, corneal graft rejection, ocular neovascularization, retinal neovascularisation, diabethic retinopathy, retrolental fibroplasia, neovascular glaucoma, gastric ulcer, infantile hemaginomas, angiofibroma of the nasopharynx, avascular necrosis of the bone and endometriosis.

15. Medicament according to one or more of claims 12-14 for the prophylaxis and/or treatment of pain.

16. Medicament according to one or more of claims 12-14 for the prophylaxis and/or treatment of inflammation.

17. Medicament according to one or more of claims 12-14 for the prophylaxis and/or treatment of inflammation related disorders, whereby said inflammation-related disorders may preferably be selected from the group consisting of arthritis, rheumatoid arthritis, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus, juvenile arthritis, rheumatic fever, symptoms associated with influenza or other viral infections, common cold, lower back pain, neck pain, dysmenorrhea, headache, toothache, sprains, strains, myositis, neuralgia, synovitis, gout, ankylosing spondylitis, bursitis, edema, inflammations following dental procedures, inflammations following dental procedures, vascular diseases, migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodkin`s disease, sclerodoma, type I diabetes, myasthenia gravis, sarcoidosis, nephrotic

syndrome, Behcet`s syndrome, polymyositis, gingivitis, hypersensivity, conjunctivitis, swelling ocurring after injury and myocardia ischemia.

18. Use of at least one substituted azetidine compound according to one or more of claims 1-10 and optionally one or more pharmaceutically acceptable excipients, for the preparation of a medicament for the inhibition of Cyclooxygenase-1, for the prophylaxis and/or treatment of Cyclooxygenase-1 related disorders, for the inhibition of Cyclooxgenase-2 and/or for the prophylaxis and/or treatment of Cyclooxygenase-2 related disorders.

19. Use of at least one substituted azetidine compound according to one or more of claims 1-10 and optionally one or more pharmaceutically acceptable excipients for the prophylaxis and/or treatment of pain, for the prophylaxis and/or treatment of inflammation and/or for the prophylaxis and/or treatment of inflammation related disorders, whereby said inflammation-related disorders may preferably be selected from the group consisting of arthritis, rheumatoid arthritis, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus, juvenile arthritis, rheumatic fever, symptoms associated with influenza or other viral infections, common cold, lower back pain, neck pain, dysmenorrhea, headache, toothache, sprains, strains, myositis, neuralgia, synovitis, gout, ankylosing spondylitis, bursitis, edema, inflammations following dental procedures, inflammations following dental procedures, vascular diseases, migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodkin`s disease, sclerodoma, type I diabetes, myasthenia gravis, sarcoidosis, nephrotic syndrome, Behcet`s syndrome, polymyositis, gingivitis, hypersensivity, conjunctivitis, swelling ocurring after injury and myocardia ischemia, for the prophylaxis and/or treatment of asthma, for the prophylaxis and/or treatment of bronchitis, for the prophylaxis and/or treatment of tendinitis, for the prophylaxis and/or treatment of bursitis, for the prophylaxis and/or treatment of skin related conditions, whereby said skin related conditions may preferably be selected from the group consisting of psoriasis, eczema, burns and dermatitis, for the prophylaxis and/or treatment of gastrointestinal disorders, whereby said gastrointestinal disorders may preferably be selected from the group consisting of inflammatory bowel disease, Crohn`s disease, gastritis, irritable bowel syndrome

and ulcerative colitis, or for treatment of fever, or for the prophylaxis and/or treatment of cancer or a cancer-related disorders, whereby said cancer or related disorder may preferably be selected from the group consisting of brain cancer, bone cancer, epithelial cell-derived neoplasia (epithelial carcinoma), basal cell carcinoma, adenocarcinoma, gastrointestinal cancer, lip cancer, colon cancer, liver cancer, bladder cancer, pancreas cancer, ovary cancer, cervical cancer, lung cancer, breast cancer, skin cancer, squamous cell cancer, prostate cancer, renal cell carcinoma and other known cancers that effect epithelial cells throughout the body, for the prophylaxis and/or treatment of polyps, for the prophylaxis and/or treatment of angiogenesis mediated disorders, preferably selected from the group consisting of metastasis, corneal graft rejection, ocular neovascularization, retinal neovascularisation, diabethic retinopathy, retrolental fibroplasia, neovascular glaucoma, gastric ulcer, infantile hemaginomas, angiofibroma of the nasopharynx, avascular necrosis of the bone and endometriosis.

20. Use of at least one substituted azetidine compound according to one or more of claims 1-10 and optionally one or more pharmaceutically acceptable excipients for the prophylaxis and/or treatment of pain.

21. Use of at least one substituted azetidine compound according to one or more of claims 1-10 and optionally one or more pharmaceutically acceptable excipients for the prophylaxis and/or treatment of inflammation.

22. Use of at least one substituted azetidine compound according to one or more of claims 1-10 and optionally one or more pharmaceutically acceptable excipients for the prophylaxis and/or treatment of inflammation related disorders, whereby said inflammation-related disorders may preferably be selected from the group consisting of arthritis, rheumatoid arthritis, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus, juvenile arthritis, rheumatic fever, symptoms associated with influenza or other viral infections, common cold, lower back pain, neck pain, dysmenorrhea, headache, toothache, sprains, strains, myositis, neuralgia, synovitis, gout, ankylosing spondylitis, bursitis, edema, inflammations following dental procedures, inflammations following dental procedures, vascular diseases, migraine headaches, periarteritis nodosa,

thyroiditis, aplastic anemia, Hodkin`s disease, sclerodoma, type I diabetes, myasthenia gravis, sarcoidosis, nephrotic syndrome, Behcet`s syndrome, polymyositis, gingivitis, hypersensivity, conjunctivitis, swelling ocurring after injury and myocardia ischemia.